UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,093	11/01/1999	PETER RICHARD REEVES	23541-01	6333

23373 7590 02/11/2005

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 02/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/423,093	REEVES ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85-106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 85-106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

3. For convenience, claim 85 is produced below.

Claim 85. (Currently Amended) A method of testing a sample for the presence of *E. coli* expressing the bacterial polysaccharide O-antigen serotype 0111, the method comprising the steps of:

(a) providing genomic DNA of a sample to be tested;

(b) providing at least one oligonucleotide molecule which is specific to said O-antigen serotype 0111, wherein said oligonucleotide molecule is ~~at least~~ about 10 to 28 nucleotides in length, and hybridizes using high stringent wash conditions to a nucleic acid sequence selected from the group consisting of:

wbdH (nucleotide positions 739 to 1932 of SEQ ID NO: 1);

wzx (nucleotide positions 8646 to 9911 of SEQ ID NO: 1);

wzy (nucleotide positions 9901 to 10953 of SEQ ID NO: 1); and

wbdM (nucleotide positions 11821 to 12945 of SEQ ID NO: 1),

wherein said high stringent wash conditions consists of 3 x 5 min washes in 2 x SSC and 0.1% SDS at room temperature, a 1 hr wash in

1 x SSC and 0.1% SDS at 58°C and 15 min wash in 0.1 x SSC and 0.1% SDS at 58°C;

(c) contacting said genomic DNA with said at least one oligonucleotide molecule to permit said oligonucleotide molecule to hybridize under said high ~~stringent~~ stringent wash conditions to said nucleic acid sequence when present in said genomic DNA; and

(d) detecting any hybridized oligonucleotide molecules, wherein detection of said hybridized oligonucleotide molecules indicates the presence of said *E. coli* in said sample.

4. For purposes of examination, said claims have been interpreted an encompassing the analysis of any sample, and that the sample may not comprise any of the named organisms, *i.e.*, *Escherichia coli O111, Escherichia coli O157, Salmonella enterica OC, Salmonella enterica OB.*

5. In accordance with claims 85, 89, 93, and 97, the only independent claims currently pending in the instant application, one is to ultimately determine if the sample comprises a one of the above-identified organisms and is expressing the identified bacterial polysaccharide antigen. It is noted with particularity that the assay does not comprise any method steps, which seek to determine if the polysaccharide antigens are in fact present. Rather, the claimed methods only determine if a nucleic acid sequence, which is assumed to encode the antigens, is present in the sample. If, or example, one were to analyze a plasmid which happens to contain one of the relevant sequences, the assay, as presently claimed, would undoubtedly result in a false positive signal as the nucleic acid of interest would be present, but it is not to be found in any of the identified organisms. Additionally, using this example, the nucleic acid does not even have to be

expressed or even be in correct reading frame such that if expressed, that it would encode the desired antigen.

6. In accordance with claims 85, 89, 93, and 97, one is to hybridize "at least one oligonucleotide" to one of the identified sequences wherein "high stringent wash conditions" are used. The employment of such conditions has been construed as leaving only those duplex structures that have hybridized to one another with great specificity. In accordance with claims 85, 90, 93, and 98, one is to employ a primer pair in said step (b), yet but one of the primers is to specifically hybridize to said nucleic acid sequence. The specification has not provided the requisite full, clear, and concise description of how non-specific hybridization can take place, and remain, when using the recited stringent wash conditions.

7. Claims 88, 92, 96, and 100 each recite a listing of nucleic acids, of which but one is to be used in the claimed method. The specification does not provide a full, clear, and concise description of which of these sequences hybridize specifically, and which do not. And the specification does not provide a full, clear, and concise description of just which combinations of sequences can be used as primer pairs.

8. Rather than provide the requisite full, clear, and concise description of the claimed invention, it appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement.

9. For the above reasons, and in the absence of convincing evidence to the contrary, claims 85-106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 86, 90, 94, and 98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 86, 90, 94, and 98 are indefinite with respect to what constitutes the metes and bounds of "specifically hybridizes." Claims 87, 91, 95, 99, and 103, which depend therefrom, fail to overcome this issue and are similarly rejected.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 85-92 and 101-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salazar et al., in view of Brennan (US Patent 5,474,796), Bastin et al., Liu et al., and Fratamico et al. (US Patent 5,652,102).

17. Salazar et al., disclose a method of detecting, via hybridization, enterohemorrhagic *Escherichia coli* isolates using oligodeoxynucleotide arrays. Specifically identified are the O157 isolate.

18. Salazar et al., do not teach detecting sequences associated with *E. coli* O111 isolate.

19. Brennan, column 9, discloses an array of oligonucleotides that comprises all possible 10-mers. By default, the array comprises all nucleic acids, target and probe, that are "about 10 nucleotides in length," as is recited in each of the independent claims.

20. Bastin et al., teaches at length of the nucleotide sequence of the O antigen gene (rfb) cluster as found in *E. coli* O111. It is noted with particularity that that the "rfb" designation/name has been changed in the art to *wzx*. This meets one of the limitations of claims 85-88, and 101-106. In support of this change in designation, attention is directed to Liu, page 2102, right column, first full paragraph, wherein is stated that "[a] gene named *wzx* (previously *rfbX*..."

21. Liu et al., page 2102, right column, provide motivation in selecting sequences from the *wzx* gene as suitable probes wherein they teach that there is "little similarity even at the amino acid sequence level" between the various *E. coli* isolates. At page 2102, left column, Liu et al., teach how this antigen has been found to exhibit "extensive structural alterations" across the 50 serogroups of *Salmonella enterica* and 170 serogroups of E*scherichia coli*.

22. Fratamico et al., teach at length of conducting PCR on a wide variety of bacterial strains. As seen in Table 1, no less than 5 different strains of *E. coli* O157 were analyzed via PCR.

23. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Salazar et al., such that sequences specific to *E. coli* O111, and O157wzx gene, which are disclosed by Brennan, are used in the assay. It would have also been obvious to said ordinary artisan to have further modified said method such that those sequences of interest would be employed in an amplification reaction, *e.g.*, polymerase chain reaction, as disclosed by Fratamico.

24. Motivation for modifying such a method can be found not only in the fact that the probe, primer, and target sequences had all been isolated, and/or made (Bastin et al., and Brennan), but also in the fact that Liu et al., teaches specifically as to how the *wzx* gene, or its encoded protein, are quite strain specific. Recognizing the specificity of such a sequence, one of ordinary skill in the art would be highly motivated to devise and use probes and primers for the detection of such target sequences. Given that all of the probe and primer sequences had already been made (Brennan), the ordinary skilled artisan would have been amply motivated to undertake such an endeavor, and would have had a most reasonable expectation of success.

25. To the extent that any one part or parts of the invention are not rendered obvious by the above-cited art, such limitations are considered to be the result of routine optimization. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining

and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

26. For the above reasons, and in the absence of convincing evidence to the contrary, claims 85-92 and 101-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salazar et al., in view of Brennan (US Patent 5,474,796), Bastin et al., Liu et al., and Fratamico et al. (US Patent 5,652,102).

Conclusion

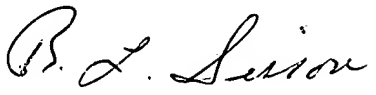
27. Rejections and/or objections that appeared in the prior Office action and not repeated hereinabove have been withdrawn.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

29. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

30. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
09 February 2005